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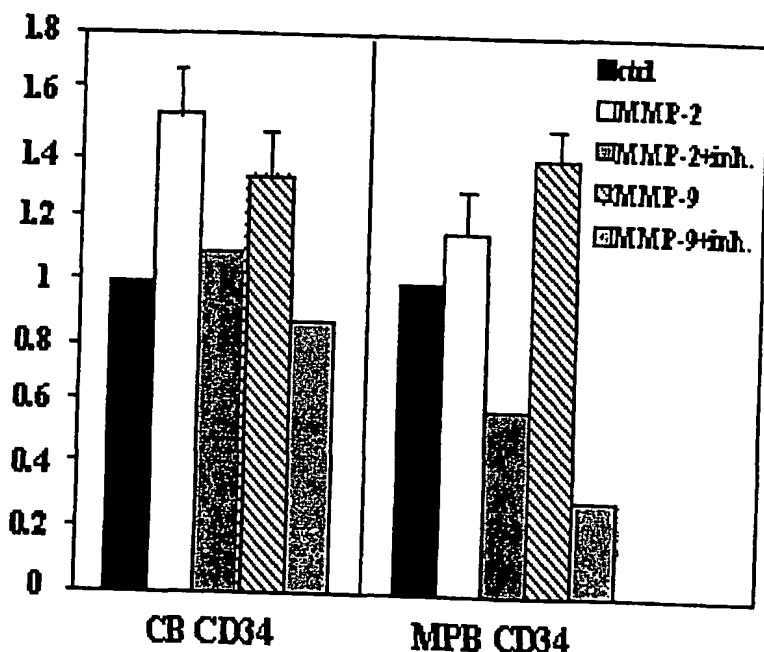
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[Continued on next page]

(54) Title: STEM CELLS HAVING INCREASED SENSITIVITY TO SDF-1 AND METHODS OF GENERATING AND USING SAME



(57) Abstract: The present invention relates to stem cells which exhibit increased sensitivity to a chemoattractant and, more particularly, to methods of generating and using them such as in clinical applications involving stem cell transplantation.

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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N5/06 A61K38/48 C12N9/64

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PETIT ISABELLE ET AL: "G-CSF induces stem cell mobilization by decreasing bone marrow SDF-1 and up-regulating CXCR4" NATURE IMMUNOLOGY, vol. 3, no. 7, July 2002 (2002-07), pages 687-694, XP002289815 ISSN: 1529-2908 the whole document ----	1-9, 54
Y	---	10-40, 47-53, 55-62 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the International filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2004/000314

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	COTTLER-FOX MICHELE H ET AL: "Stem cell mobilization." HEMATOLOGY / THE EDUCATION PROGRAM OF THE AMERICAN SOCIETY OF HEMATOLOGY. AMERICAN SOCIETY OF HEMATOLOGY. EDUCATION PROGRAM. 2003, January 2003 (2003-01), pages 419-437, XP002289816 ISSN: 1520-4391 the whole document	1-9, 54
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X	WO 03/001983 A (SINAI SCHOOL MEDICINE ; DESNICK ROBERT J (US); MARTIGNETTI JOHN ATTILI) 9 January 2003 (2003-01-09)	41-53, 59-61
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2004/000314

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LAPIDOT TSVEE ET AL: "Current understanding of stem cell mobilization: The roles of chemokines, proteolytic enzymes, adhesion molecules, cytokines, and stromal cells" EXPERIMENTAL HEMATOLOGY (CHARLOTTESVILLE), vol. 30, no. 9, September 2002 (2002-09), pages 973-981, XP002289819 ISSN: 0301-472X the whole document ---	1-40, 47-62
P, X	KOLLET ORIT ET AL: "HGF, SDF-1, and MMP-9 are involved in stress-induced human CD34+ stem cell recruitment to the liver." JOURNAL OF CLINICAL INVESTIGATION, vol. 112, no. 2, July 2003 (2003-07), pages 160-169, XP002289820 ISSN: 0021-9738 the whole document ---	1-40, 47-62
X	HUHTALA P ET AL: "COMPLETE STRUCTURE OF THE HUMAN GENE FOR 92-KDA TYPE IV COLLAGENASE DIVERGENT REGULATION OF EXPRESSION FOR THE 92-KILODALTON AND 72-KILODALTON ENZYME GENES IN HT-1080 CELLS" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 266, no. 25, 1991, pages 16485-16490, XP002315161 ISSN: 0021-9258 the whole document ---	41-46
Y	HUHTALA P ET AL: "STRUCTURE OF THE HUMAN TYPE IV COLLAGENASE GENE" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 265, no. 19, 5 July 1990 (1990-07-05), pages 11077-11082, XP002029123 ISSN: 0021-9258 the whole document ---	47-53
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2004/000314

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99/30730 A1 (UNIVERSITE LAVAL; TREMBLAY, JACQUES, P) 24 June 1999 (1999-06-24) claims; example 3 ---	41-46
X	NAGASE HIDEAKI ET AL: "Matrix metalloproteinases" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 274, no. 31, 30 July 1999 (1999-07-30), pages 21491-21494, XP002203887 ISSN: 0021-9258 the whole document	41-46
X	SUN H B ET AL: "Messenger-RNA expression of matrix metalloproteinases, tissue inhibitors of metalloproteinases, and transcription factors in rheumatic synovial cells under mechanical stimuli" BONE (NEW YORK), vol. 28, no. 3, March 2000 (2000-03), pages 303-309, XP002315162 ISSN: 8756-3282 the whole document	41-46
Y	JANOWSKA-WIECZOREK ANNA ET AL: "Growth factors and cytokines upregulate gelatinase expression in bone marrow CD34+ cells and their transmigration through reconstituted basement membrane" BLOOD, vol. 93, no. 10, 15 May 1999 (1999-05-15), pages 3379-3390, XP002315163 ISSN: 0006-4971 the whole document	47-53
Y	LOTTI FRANCESCO ET AL: "Transcriptional targeting of lentiviral vectors by long terminal repeat enhancer replacement" JOURNAL OF VIROLOGY, vol. 76, no. 8, April 2002 (2002-04), pages 3996-4007, XP002315164 ISSN: 0022-538X cited in the application the whole document	47-53

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2004/000314

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>GROTE KARSTEN ET AL: "Mechanical stretch enhances mRNA expression and proenzyme release of matrix metalloproteinase-2 (MMP-2) via NAD(P)H oxidase-derived reactive oxygen species."</p> <p>CIRCULATION RESEARCH. 13 JUN 2003, vol. 92, no. 11, 13 June 2003 (2003-06-13), pages e80-e86, XP002315165</p> <p>ISSN: 1524-4571 the whole document</p> <p>-----</p>	41-46
P, X	<p>MAGID RICHARD ET AL: "Expression of matrix metalloproteinase-9 in endothelial cells is differentially regulated by shear stress. Role of c-Myc."</p> <p>JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 278, no. 35, 29 August 2003 (2003-08-29), pages 32994-32999, XP002315166</p> <p>ISSN: 0021-9258 the whole document</p> <p>-----</p>	41-46

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2004/000314

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 10-17, 30-40, 54-58 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-40,54-62 (all completely)

A method of increasing sensitivity of stem cells to a chemoattractant, the method comprising exposing the stem cells to a matrix metalloprotease or an active portion thereof, which is capable of increasing a level of at least one chemoattractant receptor of the stem cells to thereby increase the sensitivity of the stem cells to the chemoattractant, and subject-matter related thereto.

2. claims: 41-53 (all completely)

A nucleic acid construct comprising a first polynucleotide sequence encoding a matrix metalloprotease or an active portion thereof and an inducible cis-acting regulatory element for directing expression of said polynucleotide in cells, and subject-matter related thereto.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2004/000314

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